REMARKS

Claims 1-12 and 18 presently appear in this case. Claims 9 and 11 have been withdrawn from consideration. No claims have been allowed. The official action of September 8, 2006, has now been carefully studied. Reconsideration and allowance are hereby respectfully urged.

Briefly, the present invention relates to a method for inhibiting aggregation of β-amyloid in a human subject or disaggregating aggregated β-amyloid in a human subject. To do this, an effective amount of a filamentous bacteriophage that displays an epitope of human β-amyloid is administered so as to elicit antibodies against that epitope in the subject. The antibodies that are displayed must be ones that inhibit aggregation of β-amyloid and/or cause disaggregation of β-amyloid. Preferably, the phage is administered intranasally to facilitate passage through the blood-brain barrier.

It is noted that the examiner has repeated the election requirement and it is further noted that the examiner has again stated that upon indication of allowable subject matter rejoinder may be possible.

It is further noted that the examiner still believes that claims 5 and 7 are not supported by the disclosure of the provisional application. However, it is not understood why the examiner states that the effective filing date for these

claims is July 15, 2003, particularly as the examiner has conceded that the present application is a continuation of application 09/473,653 filed December 29, 1999. As all support in the present application also appears in the application of which the present application is a continuation, the examiner should acknowledge that these claims are entitled at least to the priority date of December 29, 1999. However, as no intervening references are cited, applicant takes no position on whether or not the claims are supported by the provisional application, without prejudice toward advancing such arguments when and if an intervening reference is cited.

Claims 1-8, 10 and 12 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-20 of co-pending application no. 11/073,526. The examiner has noted applicants request of June 29, 2006, that the double patenting rejection be held in abeyance until such time that a notice of allowance is issued.

Applicant hereby continues its request that this rejection be held in abeyance until such time that a notice of allowance is issued.

Claims 1, 8 and 12 have been rejected under 35 U.S.C. 102(a) as being anticipated by the Schenk PCT

publication and under 35 U.S.C. 102(e) as being anticipated by the corresponding Schenk U.S. patent. These identical disclosures will henceforward be collectively referred to as Schenk. In response to applicant's arguments that Schenk does not explicitly teach administration of bacteriophage, *per se*, as a delivery vehicle, the examiner states that as phage is a virus it falls within the generic language of Schenk in which the use of a virus as a carrier material is disclosed, particularly in view of the fact that Schenk recognizes the existence of phage libraries for displaying peptides when evaluating compounds. The examiner also states that the screening of the compounds is noted at page 17 to be possible *in vivo*, in transgenic animals, for example. Thus, the examiner states that the screening protocol itself involves the *in vivo* administration of bacteriophage constructs that display β-amyloid peptides on their surface, and thus is itself an anticipation of claim 1. This rejection is respectfully traversed.

As stated in MPEP 2131, a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. The present claims all require that the Aβ-epitope be administered while being displayed on a filamentous bacteriophage. Schenk does not specifically disclose

administering filamentous bacteriophage displaying an Aβ-epitope as a vaccine in human therapy. It is true that Schenk generically refers to display on a virus, but the long list of viruses that is provided by Schenk does not include bacteriophage. While it is true that Schenk mentions bacteriophage in a totally different context, i.e., in selecting the appropriate epitope, there is no explicit disclosure anywhere in Schenk of use of bacteriophage as the display virus in a vaccine that is administered to humans. In an anticipation rejection, the issue is not whether it is obvious to use bacteriophage as the virus disclosed by Schenk, but whether Schenk explicitly discloses each and every element as set forth in the claim, including the use of a bacteriophage displaying epitopes as a vaccine for human administration. A genus does not necessarily anticipate a claim to a species within the genus (MPEP 2131.02). Bacteriophage is not even among the preferred viruses disclosed by Schenk. Thus, one would not immediately envision the use of bacteriophage as the carrier virus and this feature cannot be considered to be anticipated by Schenk.

An anticipation rejection cannot be overcome by showing of unexpected results. The examiner has also made an obviousness rejection of these claims using the Schenk reference as one of the references. This rejection can be

overcome by a showing of unexpected results as discussed below. However, in view of the fact that there is no explicit teaching of administration of an Aβ-epitope displayed on a filamentous bacteriophage as a therapeutic vaccine for human patients, Schenk cannot be said to anticipate the present invention.

With respect to the disclosure at page 17 of Schenk that the examiner says can also be considered to be an anticipation, it appears that the examiner is referring to the sentence at page 17, lines 23-26, where it states:

> Compounds can then be tested for prophylactic and therapeutic efficacy in transgenic animals predisposed to an amyloidogenic disease, as described in the Examples.

However, the "compounds" referred to therein are not bacteriophage displaying peptides. They are the peptides that are discovered using the phage display peptide libraries. Once a phage displayed library is screened and a peptide is identified, that peptide can then be synthesized and used therapeutically in transgenic animal models. There is no statement anywhere in Schenk that the compounds being tested in transgenic animals are displayed on bacteriophage. It is stated in the beginning of that same paragraph on page 17 of Schenk that the combinatorial libraries, admittedly including peptide libraries generated by phage display methods, are only

used for the initial screen. It is the compounds that are identified by such screens that are further analyzed, including testing in transgenic animals, not the entire phage. Note that the examples of Schenk analyze identified compounds and not entire phage.

New claim 18 has now been added to specify that the method involves administration to human subjects and that the epitope is that of a human β-amyloid. These features are supported, for example, by paragraphs [0095] and [0194]. Thus, claim 18 is not anticipated by tests on transgenic animals, even if Schenk disclosed use of the administration of phage for such a purpose (which it does not).

For all of these reasons, reconsideration and withdrawal of this anticipation rejection are respectfully urged.

Claims 1-8, 10 and 12 have been rejected under 35 U.S.C. 103(a) as being unpatentable over the Schenk references, each alternatively, in view of Devlin, Willis and Bhardwaj. The examiner states that the secondary references teach the selection of bacteriophage species fd or M13 as in claims 4 and 7 having the properties of the limitations of claims 2 and 3. This rejection is respectfully traversed.

The examiner relies solely on Schenk for the obviousness of use of a filamentous bacteriophage in general

as the carrier for an epitope of human β-amyloid in a method for inhibiting aggregation of β-amyloid or disaggregating aggregated β-amyloid in a human subject. The examiner agrees that the secondary references add nothing to the obviousness of actually using filamentous phage as the vaccine carrier, allegedly disclosed by Schenk. However, as discussed above, Schenk does not disclose administration of an Aβ-amyloid epitope displayed on the coat of a filamentous bacteriophage.

The examiner's attention is invited to the discussion of the Schenk patent at pages 5-8 of the present specification. Note particularly paragraph [0016], particularly with respect to the amount of serum titers and the degree to which these serum titers will persist over time. It has been disclosed in the present specification, see, for example, Figure 21 and Example 9, that injection of phage-carrying epitope elicits a long lasting serum titer of antibodies. This unexpected property is not suggested by any combination of the references of record.

Furthermore, the ability of phage administered intranasally to bypass the blood-brain barrier is not suggested by any of the references of record. See Example 7, beginning at page 86 of the present specification. The fact that Schenk mentions intranasal delivery among every other possible type of delivery does not suggest the results

obtained by the present invention when using intranasal delivery of filamentous phage, nor is this disclosed by any secondary references. Accordingly, claim 12, requiring administration to the olfactory system of the subject, is particularly free of this rejection.

In view of these unexpected results, any case of *prima face* obviousness has been rebutted. Reconsideration and withdrawal of this rejection are therefore respectfully urged.

Claims 1-8, 10 and 12 have been rejected under 35 U.S.C. 103(a) as being unpatentable over the Schenk references, Frenkel, Fanutti, and Delmastro in view of Bhardwaj and as evidenced by Winter. The examiner states that Frenkel teaches anti-aggregating antibodies that bind to an epitope located as a continuous sequence at the beginning of the N-terminal of β-AP. The examiner states that Fanutti and Delmastro teach the *in vivo* administration of filamentous phage as a vaccine to stimulate immunity, including intranasal administration, and that Bhardwaj teaches display on the pVIII coat proteins of phage M13. The examiner states that a combination of these references makes the present invention obvious. This rejection is respectfully traversed.

Delamstro and Fanutti add nothing to the deficiencies of Schenk as discussed above in response to the previous obviousness rejection. The unexpected results

relating to the long lasting serum titer of antibodies is not suggested by Delmastro or Fanutti. Accordingly, the present invention as a whole would not have been obvious from this large combination of references. Reconsideration and withdrawal of this rejection for the same reasons as discussed above with respect to the previous obviousness rejection are therefore respectfully urged.

It is submitted that all the claims now present in the case clearly define over the references of record and fully comply with 35 U.S.C. 112. Reconsideration and allowance are therefore earnestly solicited.

Respectfully submitted,

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